We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

5,300
Open access books available

130,000
International authors and editors

155M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS BOOK CITATION INDEX INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Evaluation and Treatment of Elevated Temperature in the Emergency Department

Marina Boushra

Abstract

Elevated patient temperature is a common vital sign abnormality in the emergency department that can be caused either by fever or hyperthermia. Fever is a frequent presentation, most commonly caused by infections of the respiratory or urinary tracts. Other occult sources include musculoskeletal, cardiac, neurological, and intra-abdominal infections. These infections can become complicated by sepsis and septic shock, conditions with high mortality. Treatment of the febrile acutely-ill patient should begin with fluids, antimicrobials, and source control. However, if this is ineffective or if the presentation is inconsistent with infection, consideration should be given to hyperthermia, rather than fever, being the cause of the patient's elevated temperature. Several life-threatening and reversible conditions can mimic sepsis and present with elevated temperature. These mimics include toxicity from medications and illicit substances, neuroleptic malignant syndrome, malignant hyperthermia, and thyroid storm. Identification of these mimics as the source of elevated temperature can lead to earlier diagnosis and improved outcomes in these patients.

Keywords: fever, hyperthermia, sepsis, overdose, infection

1. Introduction: fever vs. hyperthermia

Elevated core body temperature is a common vital sign abnormality in the emergency department (ED) that can be caused by fever or hyperthermia. While both *fever* and *hyperthermia* describe a state of elevated core temperature, they are pathophysiologically distinct clinical entities with different underlying pathologies and treatments. Fever is defined as an elevated body temperature that occurs secondary to a normal thermoregulatory system functioning at a higher set point in response to a stimulus, most commonly infection or inflammation [1]. In contrast, hyperthermia causes elevated body temperature through primary dysfunction of the hypothalamic thermoregulatory system itself [1]. Fever accounts for the vast majority of cases of elevated core temperature presentations in the ED, while hyperthermia is much more rare [1, 2]. Distinguishing between fever and hyperthermia may be difficult on initial patient presentation to the ED but the distinction has important implications for patient treatment and outcomes.

2. Fever

Fever results from a pyrogen-mediated alteration in the set point of the thermoregulatory system in the anterior hypothalamus [1]. The interaction of endogenous and exogenous pyrogens with the hypothalamus results in increased production of prostaglandins, which act on temperature-sensitive neurons and lead to increased core temperature [1] Infection is the most common cause of fever, accounting for 74% of fevers in hospitalized patients [3]. Other processes that produce endogenous pyrogens, such as malignancy and ischemia, account for the majority of the remaining sources of fever in hospitalized medical patients [4].

2.1 Sepsis

2.1.1 Definition of sepsis and septic shock

Despite significant emphasis by the Centers of Medicare and Medicaid Services (CMS) on the rapid identification and treatment of sepsis, there is no gold standard definition for the spectrum of sepsis syndromes. In actuality, sepsis is a complex and poorly understood process despite two centuries of research into its mechanisms. Sepsis is thought to result from a dysregulated and overexaggerated immune response to infection [5]. However, the complexity of sepsis and the variability in its presentation has thus far defied the creation of a gold standard definition, despite nearly three decades of attempts. The first definition of sepsis spectrum disorders was published in 1992 as a joint consensus statement between the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) [6]. This first consensus definition defined the presence sepsis spectrum disorders on elements of the patient's systemic inflammatory response syndrome (SIRS) (**Table 1**) [6]. This definition had poor sensitivity and specificity for sepsis spectrum disorders, and multiple guidelines have since attempted to revise these initial definitions, with variable success in increasing the sensitivity and specificity. The most recent consensus definition, Sepsis-3, was published in 2016 by SSCM and the European Society of Intensive Care Medicine (ESCIM) and defined the sepsis spectrum disorders by the presence of infection and two or more elements of the quick Sequential Organ Failure Assessment (qSOFA) [7]. The Sepsis-3 consensus definitions are outlined in **Table 2** below [7].

SIRS	Two or more of the following: Temperature > 38°C or < 36°C Heart rate > 90 beats per minute Respiratory rate > 20 breaths per minute or PaCO2 < 32 mmHg White blood cell count >12,000 cu/mm, <4000 cu/mm, >10% bands
Sepsis	Two SIRS criteria in the setting of known or suspected infection.
Severe sepsis	Sepsis and end-organ dysfunction
Septic shock	Sepsis with a systolic blood pressure < 90 mmHg or > 40 mmHg decrease in baseline systolic blood pressure

Table 1.
Defining sepsis based on systemic inflammatory response syndrome (SIRS): Adapted from the 1992 ACCP/SCCM consensus statement [6].

qSOFA	Altered mental status
	Systolic blood pressure < 90 mmHg
	Respiratory rate ≥ 22 breaths per minute

Table 2.
Quick sequential organ failure assessment criteria (qSOFA) [7]: sepsis-3 defines sepsis as infection with two or more of the components listed below.

2.1.2 Guidelines for the management of sepsis spectrum disorders

The Surviving Sepsis Campaign (SSC) guidelines offer recommendations for the resuscitation of patients with suspected sepsis spectrum disorders [8]. However, while these guidelines can provide an overview for the care of these patients, treatment should always be primarily guided by repeated clinical assessment and reassessment of these patients. Current guidelines recommend the continuous administration of crystalloid fluids as long as hemodynamic factors continue to improve [8] If 30 ml/kg ideal body weight (IBW) balanced crystalloid fluids does not achieve a MAP ≥65 mm Hg, a vasoactive agent should be started [8]. Norepinephrine is currently the vasopressor of choice patients with septic shock [8]. The cornerstone of management of sepsis spectrum disorders is prompt source control through administration of antimicrobials or, if necessary, surgical intervention [8]. Cultures should be collected before the first dose of antimicrobial medications; culture collection should not delay source control interventions [8]. In the emergency department, early broad-spectrum antimicrobial therapy should be initiated based on the pathogen profile of the suspected site of infection, the patient's prior culture results and susceptibilities, and local pathogen prevalence and resistance patterns. The spectrum of the antimicrobial agents can be narrowed as culture results become available or the patient presentation changes. Input from clinical pharmacists in the ED can assist in optimizing the initial antimicrobial choice and has been shown to decrease time to antibiotic administration, improve antibiotic stewardship, and improve patient outcomes [9–12].

2.2 Common sources: respiratory and urinary tract

Infections of the lower respiratory and urinary tracts comprise the majority of sepsis presentations to the ED. Community-acquired pneumonia (CAP) can be caused by a variety of bacterial and viral pathogens, with *Strepotococcus pneumoniae* being the most common bacterial etiology in those requiring hospitalization [13]. Other commonly implicated organisms include *Haemophilus influenzae, Mycoplasma pneumoniae,* and respiratory viruses. In patients requiring admission to a critical care unit, *S. pneumoniae* is still the most common etiologic organism but *Legionella pneumophila, Staphylococcus aureus,* gram-negative bacilli and influenza virus are more common [14]. Risk factors for drug resistance in CAP include age > 65, alcoholism, medical comorbidities, immunocompromise, immunosuppressive medication use, and use of beta-lactam, macrolide, or fluorquinolone antibiotics in the last 3–6 months [15]. Patients with hospitalization within three months have increased risk for hospital-acquired pneumonia with nosocomial organisms and their antibiotic regimens should include adequate coverage for *Staphylococcus aureus* and *Psuedomonas auerginosa,* which are more common in this population [15].

Infections of the urinary tract account for 40% of cases of nosocomial sepsis and the risk of infection is greatest in patients with structural or functional genitourinary abnormalities [16]. Sepsis from urinary source is more common in females [17].

Uncomplicated cystitis and pyelonephritis in women is typically caused by *Escherichia coli,* though *Proteus mirabilis, Klebsiella pneumoniae,* and *Streptococcus saprophyticus* are also relatively common [18]. As such, empiric treatment for uncomplicated urinary tract infections is best tailored to the regional *E. coli* sensitivities [18]. A complicated urinary tract infection is one which is associated with a condition that increases the risk for therapeutic failure [19]. These risk factors include diabetes, pregnancy, ureterolithiasis, renal failure, >7 days of symptoms, or an indwelling urinary device [19]. The microbial spectrum of complicated UTI is more varied and includes not only the typical organisms associated with uncomplicated UTI but also *Pseudomonas, Staphylococcus*, and *Serratia* species as well as fungi [19]. Complicated lower urinary tract infections may be managed as an outpatient; indications for hospitalization include inability to tolerate oral therapy or suspected infection with an organism resistant to oral therapies, such as extended-spectrum beta-lactamase producing organisms (ESBLs) [19].

2.3 Musculoskeletal

A comprehensive physical examination is of utmost importance in patients with a potential musculoskeletal infection as laboratory evaluation in these patients is generally non-diagnostic. Poor circulation and neuropathy are important risk factors for the development of musculoskeletal infections, and, as such, patients may not be able localize the source of their infection. Examination should include turning the patient to examine the back, palpation of the large joints, and examination of the feet and genitourinary regions for skin changes, which are often the only clue to the presence of a musculoskeletal infection [20, 21]. Comparison with the contralateral side can help to provide a baseline with which to compare for abnormalities. Practitioners should also evaluate for the presence of decubitus ulcers, which can become a nidus for osteomyelitis or bacteremia. Crepitus or pain out of proportion to examination should prompt concern for necrotizing soft tissue infection. Erythema, swelling, or pain with passive motion in a joint are concerning for a septic joint, with the knee and hip being the most common sources [22]. Risk factors for musculoskeletal infections include vasculopathy, diabetes, surgery, and immunocompromise [20]. *Staphylococcus aureus* or *Streptococcus pyogenes*-associated cellulitis is the most common cause of sepsis secondary to musculoskeletal infection [20]. While magnetic resonance imaging (MRI), surgical pathology, or culture is often necessary for the definitive diagnosis of most musculoskeletal infections, this should not delay early and aggressive source control in the ED.

2.4 Cardiac

Infectious pericarditis, myocarditis, and endocarditis as causes of sepsis can be easily missed in the emergency department due to their often subtle and variable presentations. Acute infectious pericarditis describes infection of the fibrous tissue encasing the heart and the base of the aorta and vena cava. Echoviruses and coxsackie A and B viruses account for nearly 90% of cases of infective pericarditis, with bacterial, parasitic, and fungal organisms accounting for the minority of cases [23]. The most common bacterial pathogens implicated in infective pericarditis are *Streptococcus pneumoniae* and *Staphylococcus auresus* [23]. The diagnosis of acute pericarditis is based on the presence of characteristic chest pain and electrocardiographic abnormalities [23]. Auscultation of a friction rub is helpful but is poorly sensitive for the diagnosis [24]. Infective myocarditis describes infection of the myocardial tissue, with coxsackie B being the most common cause. Other common causes include influenza virus, adenovirus, hepatitis C virus, parvovirus

B-19, and cytomegalovirus [23]. Infectious myocarditis should be considered in patients presenting with chest pain and signs of heart failure, especially when there is concurrent fever. Finally, the presence of a new murmur in an acutely ill patient should raise suspicion for infective endocarditis (IE), infection of endocardial lining of the heart valves. Important risk factors for endocarditis include intravenous drug use, prosthetic valves, indwelling intravascular devices, and immunocompromise [25]. IE presents remarkably variably and symptoms depend on the stage of disease. Fever is the most common symptom of IE; other findings concerning for endocarditis include stigmata of peripheral thromboembolism such as Osler nodes, Janeway lesions, Roth spots, or splinter hemorrhages [25]. Patients with IE may also present initially with complications of endocarditis, which include cerebrovascular ischemia or hemorrhage, septic emboli, and metastatic infection.

2.5 Meningitis and encephalitis

Meningitis is an infection of the meningeal lining of the central nervous system by bacteria, viruses, or fungi, with bacterial causes accounting the highest global burden [26]. Encephalitis describes infection of the cerebral parenchyma with a pathogen. *Streptococcus pneumonia,* group B streptococci, and *Neisseria meningitidis* are the most common causes of bacterial meningitis, with *Listeria monocytogenes* also being common in children, immunocompromised individuals, and adults greater than 50 years of age [26, 27]. Common viral causes of meningitis and encephalitis include herpesviruses, enteroviruses, and cytomegalovirus [28]. Fever, altered mental status, and nuchal rigidity are the classically described triad of meningitis, but the majority of patients in clinical practice only manifest one or two of these symptoms [26]. Lumbar puncture with cerebrospinal fluid (CSF) analysis is the diagnostic test of choice for meningitis. CT imaging should precede lumbar puncture in patients whose symptoms may be secondary to mass effect, such as those with immunocompromise, new seizure, papilledema, focal neurologic deficit, or altered mental status [26, 28, 29] Importantly, diagnostic studies should not delay the administration of antimicrobials in patients with suspected meningitis or encephalitis. Administration of antimicrobials prior to lumbar puncture has been shown to have minimal effect on chemistry and cytology findings studies of CSF but may lead to a falsely negative Gram stain or culture [30–32]. This should not affect the decision to start empiric antibiotics early in these patients.

2.6 Spinal column infections

Infections of the spinal column are an important diagnostic consideration in all patients presenting to the ED with back pain. Potential sources of infection in the spinal column include vertebral osteomyelitis, discitis, and epidural abscess. These infections are commonly missed, as there is remarkable variability in patient presentation and fever is seen in only half of these patients [33–35] Neurologic deficits likewise may or may not be present [33–35]. Risk factors for infections of the spinal column include immunocompromise, recent instrumentation, spinal implants, and use of intravenous drugs [35]. Magnetic resonance imaging (MRI) is the preferred imaging study in patients with suspected spinal column infection [35]. If MRI is unavailable, CT myelography can also be used [35].

2.7 Intraabdominal infections

Causes of intraabdominal sepsis include abdominal and pelvic abscesses, pelvic inflammatory disease, spontaneous bacterial peritonitis, cholecystitis or

cholangitis, ruptured hollow viscus, or infection of the gastrointestinal tract. While abdominal sources for sepsis are common in the ED, the diagnosis may be hampered by examination difficulties secondary to the patient's mental status or body habitus. Altered consciousness can impede a patient's ability to localize their discomfort, and many abdominal pathologies have no manifestations on external visual examination. As such, a thorough abdominal examination is of vital importance in altered patients. Although these patients may be unable to verbalize discomfort, absent bowel sounds, abdominal distention, or abdominal rigidity on examination can be clues to the presence of intraabdominal pathology [36–38]. Additionally, grimacing, guarding, or reflex tachycardia can be useful indicators of pain in patients are altered or obtunded [36–38]. Pelvic examination should be done if a pelvic source is suspected or if there is concern for toxic shock syndrome secondary to a retained vaginal foreign body [38].

2.8 Indwelling devices

Indwelling devices such as urinary catheters, ports, pacers, and long-term intravenous access are associated with an increased risk of infection. Examination of these devices is an important part of the physical examination of the septic patient. Erythema or purulence at the exit site is specific for infection but these signs of not sensitive for the presence of device-associated infection. In fact, less than 5% of dialysis line-associated bacteremia was found to have associated purulent exit site drainage [39]. Because physical examination findings are often absent, it is important to keep device-associated infection in the differential in septic patients. If infection is suspected, the device should be removed as soon as clinically possible and cultured [39–41].

3. Hyperthermia

While a reflexive diagnosis of sepsis is tempting for the ill-appearing patient with an elevated temperature, it is important to consider conditions that mimic sepsis which are often both life-threatening and reversible. Unlike the fever associated with sepsis, the majority of these sepsis mimics have elevated temperature as a result of hyperthermia, which occurs secondary to dysfunction of the hypothalamic thermoregulatory system [1]. If an infectious source cannot be found in a seemingly septic patient or the patient is not improving with antibiotics and fluids, it is important to broaden the differential to conditions that cause hyperthermia (**Table 3**).

3.1 Neuroleptic malignant syndrome (NMS)

NMS is a life-threatening syndrome of altered mental status, autonomic instability, hyperthermia, and muscle rigidity associated with the use of dopaminergic antagonists. "Lead pipe" rigidity is the hallmark physical examination finding in NMS and can be severe enough to precipitate rhabdomyolysis. Most commonly, NMS occurs with the use of dopaminergic antagonists used in the treatment of psychiatric disorders and nausea, but NMS can also be precipitated by may be caused withdrawal from dopaminergic medications, such as those used in the treatment of Parkinson's disease [42, 43]. First generation antipsychotic medications are the most commonly implicated in NMS, with haloperidol and fluphenazine having the highest risk [42]. Risk factors for the development of NMS include higher medication doses, recent or rapid dose escalation, and parenteral medication administration [42].

Condition	Presentation	Management
Neuroleptic malignant syndrome	Delirium, hyperthermia, tachycardia, rigidity	Supportive, dantrolene sodium, bromocriptine
Serotonin syndrome	Delirium, hyperthermia, tachycardia, hyperreflexia/clonus.	Supportive, consider cyproheptadine
Malignant hyperthermia	Hyperthermia, tachycardia, hypercarbia, muscle rigidity in the setting of volatile anesthetic or depolarizing muscle relaxants	Dantrolene sodium, cooling measures, treatment of hyperkalemia
Salicylate toxicity	Delirium, hyperthermia, tachycardia, hyperpnea, gastrointestinal irritation, tinnitus, triple acid–base disturbance	Sodium bicarbonate
Anticholinergic toxicity	Delirium, tachycardia, dilated nonreactive pupils, urinary retention, anhidrotic hyperthermia	Supportive
Sympathomimetic toxicity or withdrawal from sympathetic antagonists	Delirium, tachycardia, hyperthermia, hypertension, dilated reactive pupils	Benzodiazepines
Thyroid storm	Tachycardia, hyperthermia, agitation, lid-lag, ophthalmopathy, hand tremor.	Beta-blocker, thionamide, steroids
Non-exertional heat stroke	Fever, tachycardia, neurologic manifestations	Evaporative and convective cooling

Table 3.
Hyperthermic sepsis mimics, their presentation, and their management.

The highest risk of NMS is within two weeks of medication initiation but this syndrome develop at any time during the treatment timeline [44]. A review of the patient's medications is typically needed to make the diagnosis. The cornerstone of management of NMS is supportive, with discontinuation of the suspected offending agent, support of the cardiopulmonary system, maintenance of normothermia and euvolemia, and prevention of complications including deep venous thrombosis, acute renal failure, and cardiac dysrhythmias [42–44]. In cases of severe muscle rigidity not responding to supportive treatment, intravenous dantrolene sodium or oral bromocriptine mesylate should be considered [44].

3.2 Serotonin syndrome (SS)

SS is a syndrome of altered mentation, neuromuscular abnormalities, and autonomic hyperactivity caused by excess serotonin levels [45]. The most commonly implicated medications in SS include linezolid, fentanyl, and selective serotonin reuptake inhibitor (SSRIs) [46]. The neuromuscular abnormalities associated with SS can include hyperreflexia, clonus, or muscle rigidity, and, as with NMS, these may be severe enough to which may lead to rhabdomyolysis [45, 46]. SS is a clinical diagnosis based on patient presentation, and there is no laboratory test or imaging study to confirm the diagnosis [45]. The Hunter criteria for serotonin syndrome is one outline the clinical criteria needed to make the diagnosis [47]. Like NMS, management of SS is primarily supportive. If this is insufficient or ineffective, use of cyproheptadine can be used under the consultation of a toxicologist [45]. If neuromuscular paralysis is need to control neuromuscular rigidity or facilitate intubation, only nondepolarizing agents should be used, as depolarizing agents may exacerbate the hyperkalemia precipitated by the neuromuscular abnormalities of SS [45, 46].

Spontaneous clonus
Inducible clonus AND agitation OR diaphoresis
Ocular clonus AND agitation OR diaphoresis
Tremor AND hyperreflexia
Hypertonia, temperature > 38°C AND ocular OR inducible clonus

Table 4.
Hunter criteria for serotonin syndrome [47].

Suspect serotonin syndrome if the patient has taken a serotonergic agent and has one of the symptom complexes outlined below (**Table 4**).

3.3 Malignant hyperthermia (MH)

MH is a genetic disorder which results in a hypermetabolic response to volatile anesthetics and depolarizing muscle relaxants [48]. This pathologic response to these medications results from caused the release of excessive calcium from the sarcoplasmic reticulum, which leads to uncoupling of oxidative phosphorylation, the release of heat, and a rise in metabolic rate [49]. MH presents with hyperthermia, tachycardia, hypercarbia, increased oxygen consumption, and muscle rigidity following the administration of a volatile anesthetic or depolarizing muscle relaxants. In the ED, MH is most likely to present following an intubation using succinylcholine and MH should be a diagnostic consideration in a patients with acute decompensation following intubation. MH is treated with intravenous dantrolene loaded at a dose of 2.5 mg/kg followed by boluses of 1 mg/kg until symptoms resolution [48]. Aggressive cardiopulmonary support, maintenance of normothermia and euvolemia, and treatment of electrolyte derangements is likewise important.

3.4 Salicylate toxicity

Aspirin ingestion is the most common cause of salicylate toxicity, but other common sources include Oil of Wintergreen, some wart removers, and keratolytics [50]. Salicylate toxicity is an important sepsis mimic, as patients with salicylate toxicity will have tachycardia, tachypnea, elevated temperature, and lactic acidosis. These symptoms occur secondary to salicylate interference with aerobic metabolism [50]. The classically described triad of salicylate toxicity is hyperpnea, tinnitus, and gastrointestinal irritation [51]. Gastrointestinal symptoms vary and can include abdominal pain, nausea, vomiting, and diarrhea. Tinnitus associated with salicylate toxicity may be described as hearing loss rather than "ringing in the ears" by patients and may be a difficult symptom to elicit if the patient is altered or obtunded [51]. Laboratory testing in salicylate toxicity will show a classic "triple acid-base disorder." This includes a respiratory alkalosis from hyperventilation, a compensatory non-gap metabolic acidosis, and an anion-gap metabolic acidosis from secondary to lactic acid accumulation [51]. Management is through systemic alkalinization with sodium bicarbonate [52].

3.5 Anticholinergic toxicity

Anticholinergic substances are ubiquitous in both pharmaceutical compounds and nature. Commonly encountered causes of anticholinergic toxicity include ingestion of antihistamine medications, tricyclic antidepressants, jimson weed, and tainted recreational drugs. Anticholinergic toxicity can easily be mistake for sepsis,

as these patients present with high temperature, delirium, and tachycardia [53]. A distinguishing feature of anticholinergic toxicity is the presence of anhidrotic hyperthermia, in contrast to septic patients who are febrile and diaphoretic [53]. This is a result of anticholinergic blockade of sweat glands, preventing homeostatic hydrosis in response to elevated core temperature [53, 54]. Other clinical findings in anticholinergic toxicity include dry mucus membranes, dilated, non-reactive pupils and urinary retention [53]. The management of anticholinergic toxicity is primarily supportive. Benzodiazepines should be used for agitation or seizures [54]. Physostigmine, an anticholinesterase inhibitor, can be used as an antidote for anticholinergic toxicity under the consultation of a toxicologist [54].

3.6 Sympathomimetic toxicity or withdrawal from sympathetic antagonists

Overstimulation of the sympathetic nervous system can occur through direct agonism of the sympathetic receptors or withdrawal from substances that act as sympathetic antagonists [55]. Common sympathomimetic compounds encountered in the ED include cocaine, phencyclidine, and amphetamines. Withdrawal from alcohol or benzodiazepines can also result in sympathetic overstimulation [56]. Symptoms of sympathomimetic toxicity hyperthermia, tachycardia delirium, and reactive mydriasis [55]. Hyperthermia in sympathetic overstimulation results from direct agonism of alpha receptors as well as heat released by associated psychomotor agitation [55]. Benzodiazepines are mainstay of management of both sympathomimetic toxicity and withdrawal from antisympathetic agents [55].

3.7 Thyroid storm

Thyroid storm is the most severe manifestation of thyrotoxicosis and can be caused by overdose of therapeutic thyroid hormone or may present in patients with underlying thyrotoxicosis, seemingly unprovoked or may be precipitated by trauma, infection, childbirth, or other acute events [57]. Symptoms of thyroid storm include delirium, hyperthermia, diarrhea, and tachydysrhythmias, which can be severe enough to cause cardiovascular collapse and hemodynamic compromise [57, 58]. Liver failure may also occur [57]. The diagnostic laboratory abnormality in thyroid storm a severely low or undetectable thyroid stimulating hormone (TSH). Physical examination findings concerning for thyroid storm are those classically seen in hyperthyroidism and include ophthalmopathy, lid lag, thyromegaly, hand tremor, and global hyperreflexia [57, 58]. ED management of includes immediate treatment with a beta blocker, a thionamide, and glucocorticoids [59]. An iodine preparation should be given an hour after the administration of the thionamide, to prevent the iodine being used as substrate for the synthesis of more thyroid hormone [59]. If an infection is suspected as the cause of thyroid storm, broad-spectrum empiric antibiotics should be administered.

3.8 Heat stroke

Heat stroke is condition of elevated core body temperature with associated central nervous system dysfunction, commonly encephalopathy [60]. Heat stroke can be broadly divided into non-exertional and exertional. Non-exertional heat stroke classically affects older individuals with comorbidities that result in impaired thermoregulation, prevent access to adequate hydration, or inhibit removal from a hot environment [60]. In contrast, exertional heat stroke is more likely to occur in young, healthy individuals in the setting of exertion that overwhelms homeostatic thermoregulatory mechanisms. Heat stroke is a clinical diagnosis of exclusion made

based on elevated body temperature (generally >40°C), central nervous system dysfunction (classically encephalopathy), and a history of exposure to severe environmental heat or excessive exertion [60]. Evaporative and convective cooling are the treatments of choice and should be initiated as soon as the diagnosis is made to improve morbidity and mortality [61, 62]. Common cooling methods used in the ED include ice water immersion, cooled fluid lavage, and evaporative cooling [61, 62]. In cases of refractory hyperthermia, dantrolene can be used as salvage therapy but its efficacy in this clinical context is uncertain [63, 64].

4. Conclusion

Elevated core temperature can be the result of either fever or hyperthermia. Fever is mor common and is typically caused by infections of the respiratory or urinary tracts. Other potential sources of infection include musculoskeletal, cardiac, neurological, and intra-abdominal as well as infection from indwelling medical devices. Treatment of patients with elevated core temperature should begin with fluids, empiric antimicrobials, and source control. If treatment of infection is ineffective or if the presentation is inconsistent with the presence of infection, the differential diagnosis should be expanded to consider conditions that cause hyperthermia as the cause of elevated core temperature. Such sepsis mimics include toxicity from medications and illicit substances, neuroleptic malignant syndrome, serotonin syndrome, malignant hyperthermia, thyroid storm, and heat stroke. Identification of these mimics as the source of elevated temperature leads to earlier diagnosis and improved prognosis in these patients.

Author details

Marina Boushra
The Respiratory Institute at the Cleveland Clinic, Cleveland, Ohio, United States of America

*Address all correspondence to: mnb9143@gmail.com

References

[1] Walter EJ, Hanna-Jumma S, Carraretto M, Forni L. The pathophysiological basis and consequences of fever. *Critical Care*. 2016;20(1):200. doi:10.1186/s13054-016-1375-5

[2] Bartfai T, Conti B. Fever. *TheScientificWorldJournal*. 2010;10:490-503. doi:10.1100/tsw.2010.50

[3] Kaul DR, Flanders SA, Beck JM, Saint S. Brief report: Incidence, etiology, risk factors, and outcome of hospital-acquired fever: A systematic, evidence-based review. *Journal of General Internal Medicine*. 2006;21(11):1184-1187. doi:10.1111/j.1525-1497.2006.00566.x

[4] Bor DH, Makadon HJ, Friedland G, Dasse P, Komaroff AL, Aronson MD. Fever in hospitalized medical patients - Characteristics and significance. *Journal of General Internal Medicine*. 1988;3(2):119-125. doi:10.1007/BF02596115

[5] Taeb AM, Hooper MH, Marik PE. Sepsis: Current Definition, Pathophysiology, Diagnosis, and Management. *Nutrition in Clinical Practice*. 2017;32(3):296-308. doi:10.1177/0884533617695243

[6] American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Critical care medicine*. 1992;20(6):864-874. http://www.ncbi.nlm.nih.gov/pubmed/1597042. Accessed February 10, 2018.

[7] Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801. doi:10.1001/jama.2016.0287

[8] Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Medicine*. 2017;43(3):304-377. doi:10.1007/s00134-017-4683-6

[9] Cavanaugh JB, Sullivan JB, East N, Nodzon JN. Importance of Pharmacy Involvement in the Treatment of Sepsis. *Hospital Pharmacy*. 2017;52(3):191-197. doi:10.1310/hpj5203-191

[10] Moussavi K, Nikitenko V. Pharmacist impact on time to antibiotic administration in patients with sepsis in an ED. *The American Journal of Emergency Medicine*. 2016;34(11):2117-2121. doi:10.1016/j.ajem.2016.07.031

[11] Laine ME, Flynn JD, Flannery AH. Impact of Pharmacist Intervention on Selection and Timing of Appropriate Antimicrobial Therapy in Septic Shock. *Journal of Pharmacy Practice*. 2018;31(1):46-51. doi:10.1177/0897190017696953

[12] Gastmeier P, Kampf G, Wischnewski N, ... TH-J of H, 1998 undefined. Prevalence of nosocomial infections in representative German hospitals. *Elsevier*. https://www.sciencedirect.com/science/article/pii/S0195670198901736. Accessed October 13, 2020.

[13] Jain S, Self WH, Wunderink RG, et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. *The New England journal of medicine*. 2015;373(5):415-427. doi:10.1056/NEJMoa1500245

[14] Cillóniz C, Ewig S, Polverino E, et al. Microbial aetiology of community-acquired pneumonia and its relation to severity. *Thorax*. 2011;66(4):340-346. doi:10.1136/thx.2010.143982

[15] Ewig S, Welte T, Torres A. Is healthcare-associated pneumonia a distinct entity needing specific therapy? *Current opinion in infectious diseases*. 2012;25(2):166-175. doi:10.1097/QCO.0b013e32835023fb

[16] Johansen T, Cek M, Naber K, urology LS-E, 2007 undefined. Prevalence of hospital-acquired urinary tract infections in urology departments. *Elsevier*. https://www.sciencedirect.com/science/article/pii/S0302283806009365?casa_token=tx0EZL4s2ZoAAAAA:VUDyuCMPljmzF4xbstHRc1xuxmHJLjso3z8qabxrdz-BaDrAfN9Fqx3tsL1q5AlUqrpHyLLl_qU. Accessed October 13, 2020.

[17] Kalra O. Approach to a patient with urosepsis. *Journal of Global Infectious Diseases*. 2009;1(1):57. doi:10.4103/0974-777x.52984

[18] Stamm WE, Hooton TM, Hooton TM. Management of urinary tract infections in adults. *The New England journal of medicine*. 1993;329(18):1328-1334. doi:10.1056/NEJM199310283291808

[19] Nicolle LE, AMMI Canada Guidelines Committee* ACG. Complicated urinary tract infection in adults. *The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale*. 2005;16(6):349-360. http://www.ncbi.nlm.nih.gov/pubmed/18159518. Accessed December 16, 2016

[20] Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. *Clinical Infectious Diseases*. 2014;59(2). doi:10.1093/cid/ciu296

[21] Horowitz DL, Katzap E, Horowitz S, Barilla-LaBarca M-L. Approach to septic arthritis. *American family physician*. 2011;84(6):653-660. http://www.ncbi.nlm.nih.gov/pubmed/21916390. Accessed February 13, 2018.

[22] Hassan AS, Rao A, Manadan AM, Block JA. Peripheral Bacterial Septic Arthritis: Review of Diagnosis and Management. *Jcr: Journal of Clinical Rheumatology*. 2017;23(8):435-442. doi:10.1097/rhu.0000000000000588

[23] Htwe TH, Khardori NM. Cardiac emergencies: Infective endocarditis, pericarditis, and myocarditis. *Medical Clinics of North America*. 2012;96(6):1149-1169. doi:10.1016/j.mcna.2012.09.003

[24] Lange RA, Hillis LD. Acute Pericarditis. *New England Journal of Medicine*. 2004;351(21):2195-2202. doi:10.1056/NEJMcp041997

[25] Cahill TJ, Prendergast BD. Infective endocarditis. *Lancet (London, England)*. 2016;387(10021):882-893. doi:10.1016/S0140-6736(15)00067-7

[26] Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice Guidelines for the Management of Bacterial Meningitis. *Clinical Infectious Diseases*. 2004;39(9):1267-1284. doi:10.1086/425368

[27] Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. *Clinical microbiology reviews*. 2010;23(3):467-492. doi:10.1128/CMR.00070-09

[28] Logan SAE, MacMahon E. Viral meningitis. *BMJ*. 2008;336(7634):36-40. doi:10.1136/BMJ.39409.673657.AE

[29] Lucas S. Acute bacterial meningitis during and after pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2012;119(13):1555-1557. doi:10.1111/1471-0528.12025

[30] Blazer S, Berant M, Alon U. Bacterial meningitis. Effect of antibiotic treatment on cerebrospinal fluid. *American journal of clinical pathology*. 1983;80(3):386-387. http://www.ncbi.nlm.nih.gov/pubmed/6881104. Accessed February 10, 2018.

[31] Nigrovic LE, Malley R, Macias CG, et al. Effect of antibiotic pretreatment on cerebrospinal fluid profiles of children with bacterial meningitis. *Pediatrics*. 2008;122(4):726-730. doi:10.1542/peds.2007-3275

[32] Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar puncture in pediatric bacterial meningitis: defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. *Pediatrics*. 2001;108(5):1169-1174. http://www.ncbi.nlm.nih.gov/pubmed/11694698. Accessed February 10, 2018.

[33] Torda AJ, Gottlieb T, Bradbury R. Pyogenic vertebral osteomyelitis: analysis of 20 cases and review. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 1995;20(2):320-328. http://www.ncbi.nlm.nih.gov/pubmed/7742437. Accessed February 10, 2018.

[34] Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: report of nine cases and review of the literature. *Reviews of infectious diseases*. 1(5):754-776. http://www.ncbi.nlm.nih.gov/pubmed/542761. Accessed February 10, 2018.

[35] Berbari EF, Kanj SS, Kowalski TJ, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2015;61(6):e26-46. doi:10.1093/cid/civ482

[36] Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2010;50(2):133-164. doi:10.1086/649554

[37] Swenson RM, Lorber B, Michaelson TC, Spaulding EH. The Bacteriology of Intra-abdominal Infections. *Archives of Surgery*. 1974;109(3):398. doi:10.1001/archsurg.1974.01360030050013

[38] Walker CK, Wiesenfeld HC. Antibiotic Therapy for Acute Pelvic Inflammatory Disease: The 2006 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines. *Clinical Infectious Diseases*. 2007;44(Supplement 3):S111-S122. doi:10.1086/511424

[39] Troidle L, Finkelstein FO. Catheter-related bacteremia in hemodialysis patients: the role of the central venous catheter in prevention and therapy. *The International journal of artificial organs*. 2008;31(9):827-833. http://www.ncbi.nlm.nih.gov/pubmed/18924095. Accessed February 11, 2018.

[40] Sychev D, Maya ID, Allon M. Clinical Management of Dialysis Catheter-Related Bacteremia with Concurrent Exit-Site Infection. *Seminars in Dialysis*. 2011;24(2):239-241. doi:10.1111/j.1525-139X.2011.00869.x

[41] Ramanathan V, Darouiche RO. Prevention and management of hemodialysis catheter infections. *Expert Review of Anti-infective Therapy*. 2012;10(12):1447-1455. doi:10.1586/eri.12.134

[42] Adnet P, Lestavel P, Krivosic-Horber R. Neuroleptic malignant syndrome. *British Journal of Anaesthesia*. 2000;85(1):129-135. doi:10.1093/bja/85.1.129

[43] Bond W. Detection and Management of Neuroleptic Malignant Syndrome. *Clinical pharmacology*. 1984;3(302).

[44] Reulbach U, Dütsch C, Biermann T, et al. Managing an effective treatment for neuroleptic malignant syndrome. *Critical Care*. 2007;11(1):R4. doi:10.1186/cc5148

[45] Boyer EW, Shannon M. The Serotonin Syndrome. *New England Journal of Medicine*. 2005;352(11): 1112-1120. doi:10.1056/NEJMra041867

[46] Ables AZ, Nagubilli R. Prevention, recognition, and management of serotonin syndrome. *American family physician*. 2010;81(9):1139-1142. http://www.ncbi.nlm.nih.gov/pubmed/20433130. Accessed February 11, 2018.

[47] Dunkley EJC, Isbister GK, Sibbritt D, Dawson AH, Whyte IM. The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *QJM : monthly journal of the Association of Physicians*. 2003;96(9):635-642. http://www.ncbi.nlm.nih.gov/pubmed/12925718. Accessed February 11, 2018.

[48] Glahn KPE, Ellis FR, Halsall PJ, et al. Recognizing and managing a malignant hyperthermia crisis: guidelines from the European Malignant Hyperthermia Group. *British Journal of Anaesthesia*. 2010;105(4):417-420. doi:10.1093/bja/aeq243

[49] Rosenberg H, Pollock N, Schiemann A, Bulger T, Stowell K. Malignant hyperthermia: a review. *Orphanet Journal of Rare Diseases*. 2015;10. doi:10.1186/S13023-015-0310-1

[50] O'Malley GF. Emergency Department Management of the Salicylate-Poisoned Patient. *Emergency Medicine Clinics*. 2007;25(2):333-346. doi:10.1016/J.EMC.2007.02.012

[51] Bari N. Salicylate poisoning. *JPMA The Journal of the Pakistan Medical Association*. 1995;45(6):160-161. http://www.ncbi.nlm.nih.gov/pubmed/7474293. Accessed February 11, 2018.

[52] Chyka PA, Erdman AR, Christianson G, et al. Salicylate poisoning: An evidence-based consensus guideline for out-of-hospital management. *Clinical Toxicology*. 2007;45(2):95-131. doi:10.1080/15563650600907140

[53] Dawson AH, Buckley NA. Pharmacological management of anticholinergic delirium - theory, evidence and practice. *British journal of clinical pharmacology*. 2016;81(3): 516-524. doi:10.1111/bcp.12839

[54] Oakley P. Physostigmine versus diazepines for anticholinergic poisoning. *Annals of emergency medicine*. 2001;37(2):239-241. http://www.ncbi.nlm.nih.gov/pubmed/11174251. Accessed February 11, 2018.

[55] Hayes BD, Martinez JP, Barrueto F. Drug-induced hyperthermic syndromes. Part I. Hyperthermia in overdose. *Emergency Medicine Clinics of North America*. 2013;31(4):1019-1033. doi:10.1016/j.emc.2013.07.004

[56] Paden MS, Franjic L, Halcomb SE. Hyperthermia caused by drug interactions and adverse reactions. *Emergency Medicine Clinics of North America*. 2013;31(4):1035-1044. doi:10.1016/j.emc.2013.07.003

[57] Chiha M, Samarasinghe S, Kabaker AS. Thyroid Storm. *Journal of Intensive Care Medicine*. 2015;30(3): 131-140. doi:10.1177/0885066613498053

[58] Nayak B, Burman K. Thyrotoxicosis and Thyroid Storm. doi:10.1016/j.ecl.2006.09.008

[59] Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid

Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. *Thyroid*. 2016;26(10):1343-1421. doi:10.1089/thy.2016.0229

[60] Yeo TP. Heat stroke: a comprehensive review. *AACN clinical issues*. 15(2):280-293. http://www.ncbi.nlm.nih.gov/pubmed/15461044. Accessed February 11, 2018.

[61] Smith JE, Wallis L. Cooling methods used in the treatment of exertional heat illness. *British journal of sports medicine*. 2005;39(8):503-507; discussion 507. doi:10.1136/bjsm.2004.013466

[62] Gaudio FG, Grissom CK. Cooling Methods in Heat Stroke. *The Journal of Emergency Medicine*. 2016;50(4):607-616. doi:10.1016/j.jemermed.2015.09.014

[63] Moran D, Epstein Y, Wiener M, Horowitz M. Dantrolene and recovery from heat stroke. *Aviation, space, and environmental medicine*. 1999;70(10):987-989. http://www.ncbi.nlm.nih.gov/pubmed/10519477. Accessed February 11, 2018.

[64] Hadad E, Cohen-Sivan Y, Heled Y, Epstein Y. Clinical review: Treatment of heat stroke: should dantrolene be considered? *Critical Care*. 2004;9(1):86. doi:10.1186/cc2923